Complete Summary

GUIDELINE TITLE

AASLD practice guidelines: evaluation of the patient for liver transplantation.

BIBLIOGRAPHIC SOURCE(S)

Murray KF, Carithers RL Jr. AASLD practice guidelines: evaluation of the patient for liver transplantation. Hepatology 2005 Jun;41(6):1407-32. [328 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

The guideline updates a previous version: Carithers RL Jr. Liver transplantation. American Association for the Study of Liver Diseases. Liver Transpl 2000 Jan;6(1):122-35.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Chronic liver failure from:
  - Chronic noncholestatic liver disorders (e.g., hepatitis C, hepatitis B, autoimmune hepatitis, alcoholic cirrhosis)
  - Cholestatic liver disorders (e.g., primary biliary cirrhosis; primary sclerosing cholangitis; childhood cholestatic disease, including biliary atresia, Alagille syndrome, and cystic fibrosis)
  - Metabolic disorders (e.g., alpha-1-antitrypsin deficiency, Wilson disease, nonalcoholic steatohepatitis and cryptogenic cirrhosis,

hereditary hemochromatosis, neonatal hemochromatosis, tyrosinemia and glycogen storage disease
        - Metabolic disorders with severe extrahepatic manifestations (e.g., amyloidosis, hyperoxaluria, urea cycle defects, disorders of branched-chain amino acids)
- Hepatic malignancies (e.g., hepatocellular carcinoma [HCC], hepatoblastoma, fibrolamellar hepatocellular carcinoma, hemangioendothelioma, cholangiocarcinoma)
- Acute liver failure (fulminant hepatic failure [FHF]) of any cause
- Other end-stage liver disease (e.g., Budd-Chiari syndrome, metastatic neuroendocrine tumors, and polycystic disease)

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Critical Care
Gastroenterology
Infectious Diseases
Internal Medicine
Pediatrics
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide a data-supported approach to the treatment of patients considered for liver transplantation

TARGET POPULATION

Individuals with acute or chronic liver failure

INTERVENTIONS AND PRACTICES CONSIDERED

Pre-Transplantation Evaluation and Management

1. Determination of need for referral to transplant center, based on signs and symptoms, and prognosis, determined through use of tools, including Child-Turcotte-Pugh (CTP) classification, the model for end-stage liver disease (MELD), and the pediatric end-stage liver disease (PELD) model
2. Disease-specific alternative treatment
3. Evaluation for coronary artery disease (dobutamine stress echocardiography, cardiac catheterization)

4. Screening for pulmonary hypertension (Doppler echocardiography, right heart catheterization)
5. Counseling to refrain from smoking
6. Evaluation of renal function
7. Consultation with oncologist, if applicable
8. Screening for osteoporosis
9. Formation of a well-coordinated, multidisciplinary team for human immunodeficiency virus (HIV) patients
10. Careful anatomical evaluation (patients with occlusion or hypoplasia splanchnic blood supply)
11. Counseling of patients with disorders that may adversely affect postoperative compliance
12. Pre-transplant colonoscopies, as indicated
13. Assessment for congenital heart disease in children with Alagille syndrome
14. Careful assessment of lung disease in children with cystic fibrosis and in all patients with cirrhosis secondary to alpha-1-antitrypsin deficiency
15. Screening for metabolic dysregulation in patients with decompensated cryptogenic cirrhosis
16. Screening for hemochromatosis in patients with newly diagnosed cirrhosis and pretransplantation phlebotimization, if indicated
17. Cardiac evaluation for all patients with hereditary hemochromatosis

Liver Transplantation, including

1. Selection of patients for liver transplantation
2. Timing of transplantation
3. Retransplantation

Pre- and Posttransplantation Treatment/Control of Comorbidities, including

1. Medical therapy for pulmonary hypertension
2. Efforts to improve bone density and prevent pathological fractures
3. Antiviral therapy for hepatitis B and C (antiviral therapy)
4. Immunosuppressive therapy

Posttransplantation Care

1. Immunosuppressive therapy
2. Metabolic monitoring

MAJOR OUTCOMES CONSIDERED

Outcome of transplantation versus the natural history of the disease in question with respect to:

- Survival rates
- Morbidity and mortality
- Graft survival
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

These recommendations provide a data-supported approach. They are based on the following: (1) formal review and analysis of the recently published world literature on the topic [Medline search]; (2) American College of Physicians Manual for Assessing Health Practices and Designing Practice Guidelines; (3) guideline policies, including the American Association for the Study of Liver Diseases (AASLD) Policy on the Development and Use of Practice Guidelines and the American Gastroenterological Association (AGA) Policy Statement on Guidelines; (4) the experience of the authors in the specified topic.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grade I: Randomized controlled trials

Grade II-1: Controlled trials without randomization

Grade II-2: Cohort or case-control analytic studies

Grade II-3: Multiple time series, dramatic uncontrolled experiments

Grade III: Opinions of respected authorities, descriptive epidemiology

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline was produced in collaboration with the Practice Guidelines Committee of the American Association for the Study of Liver Diseases. This committee, in concert with a lead reviewer, provided extensive peer review of this manuscript.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Evidence ratings (Grades I, II-1, II-2, II-3, and III) are defined at the end of the "Major Recommendations" field.

When Should Evaluation for Transplantation Be Considered?

Determining the Need for Liver Transplantation

1. Patients with cirrhosis should be referred for transplantation when they develop evidence of hepatic dysfunction (Child-Turcotte-Pugh [CTP] >7 and model for end-stage liver disease [MELD] >10) or when they experience their first major complication (ascites, variceal bleeding, or hepatic encephalopathy) (II-3).
2. Children with chronic liver disease should be referred when they deviate from normal growth curves or develop evidence of hepatic dysfunction or portal hypertension (II-3).
3. Patients with type I hepatorenal syndrome should have an expedited referral for liver transplantation (II-3).

Exploring Alternative Forms of Treatment

4. Every option for disease-specific treatment should be considered in patients with chronic liver disease.

a. Only when there is no effective alternative therapy or when treatment has been shown to be ineffective should liver transplantation be considered (II-3).
b. However, in critically ill patients in whom the outcome of medical therapy is uncertain, it is appropriate to simultaneously begin specific treatment for the disease and to initiate evaluation for potential liver transplantation (III).

Specific Medical, Surgical, and Psychosocial Issues

5. Chronic smokers, patients over the age of 50, and those with a clinical or family history of heart disease or diabetes should undergo evaluation for coronary artery disease (III).
6. Dobutamine stress echocardiography appears to be an effective screening test in this setting; however, positive test results should be confirmed with cardiac catheterization (II-2).

The Hepatopulmonary Syndrome (HPS)

7. Because patients with cirrhosis and severe hepatopulmonary syndrome have an extremely poor prognosis without transplantation, they should have an expedited referral and evaluation for liver transplantation (II-2).

Portopulmonary Hypertension

8. All patients undergoing evaluation for potential liver transplantation should undergo screening for pulmonary hypertension (II-3).
9. Doppler echocardiography is an excellent screening test in this setting; however, positive test results should be confirmed with right heart catheterization (II-2).
10. Patients with severe pulmonary hypertension should be considered for liver transplantation only if the condition can be effectively controlled with medical therapy (II-3).

Obesity and Cigarette Smoking

11. Morbid obesity should be considered a contraindication to liver transplantation (II-3).
12. All patients considered for liver transplantation should be encouraged to undergo efforts to abstain from smoking (III).

Renal Failure

13. The presence of renal insufficiency is an important predictor of postoperative renal failure and mortality after liver transplantation, and hence a thorough pretransplantation evaluation of renal function is important (II-2).
14. Because rapidly progressive hepatorenal syndrome (type 1) has an ominous prognosis and usually is reversed by transplantation, patients with this condition should have an expedited referral for evaluation (II-3).
15. Selected patients with chronic renal and liver disease should be considered for combined liver-kidney transplantation (III).

Extrahepatic Malignancies

16. Because the natural history and chance of recurrence varies with different tumors, close consultation between a patient's oncologist and transplantation physicians should occur before evaluation for liver transplantation in patients with extrahepatic malignancies (III).

Osteoporosis

17. All patients with chronic liver disease should be screened for osteoporosis during evaluation for liver transplantation (II-3).
18. In those with significant bone loss, efforts to improve bone density and to prevent pathological fractures should be pursued both before and after transplantation (III).

Patients with Human Immunodeficiency Virus (HIV) Infection

19. Liver transplantation in patients with HIV infection requires a well-coordinated, multidisciplinary team with expertise both in transplantation and HIV management (III).

Surgical Issues

20. Patients with occlusion or hypoplasia of the splanchnic blood supply require careful anatomical evaluation before transplantation because of the increased risk of perioperative mortality and graft loss (II-3).

Psychosocial Issues

21. Individuals should meet reasonable expectations of compliance before placement on a donor waiting list (II-3).
22. However, before a candidate is refused liver transplantation, every effort should be made to provide expert counseling and treatment of disorders that may adversely affect postoperative compliance (III).
23. Patients receiving methadone maintenance who are otherwise good candidates for transplantation should not be denied consideration for the operation (II-2).

Specific Indications for Liver Transplantation

Chronic Noncholestatic Liver Disorders

Chronic Hepatitis C

24. Patients with clinically decompensated cirrhosis from chronic hepatitis C infection should be referred for consideration of liver transplantation (II-3).
25. Antiviral therapy should be considered in patients who have been accepted as candidates for liver transplantation, as long as treatment is administered by experienced clinicians, with vigilant monitoring for adverse events (II-3).
26. Treatment of hepatitis C virus (HCV)-related disease following liver transplantation should be undertaken with caution because of the increased

risk of adverse events and should be performed under the supervision of a physician experienced in transplantation (II-2).

Chronic Hepatitis B

27. Patients with decompensated cirrhosis secondary to chronic hepatitis B should be considered for treatment with antiviral therapy in coordination with the transplant center (II-3).
28. Interferon-alfa should not be used in patients with decompensated cirrhosis because of the risk of exacerbation of liver disease (II-3).
29. The posttransplantation care of patients with hepatitis B virus (HBV) should include antiviral therapy (II-3).

Autoimmune Hepatitis

30. Liver transplantation should be considered in decompensated patients with autoimmune hepatitis who are unable to undergo or be salvaged by medical therapy (II-3).
31. Due to the risk of recurrent disease and enhanced risk of rejection, patients with autoimmune hepatitis may require more immunosuppression than patients transplanted for other indications (II-3).

Alcoholic Cirrhosis

32. To be considered for transplantation, potential candidates with alcoholic liver disease should have careful assessment by a health care professional experienced in the management of patients with addictive behavior (III).
33. It is prudent to delay transplantation for a minimum of 3 to 6 months of abstinence from alcohol to avoid exposing patients who may not need transplantation to the risk of unnecessary surgery (II-2).

Cholestatic Liver Disorders

Primary Biliary Cirrhosis

34. Liver transplantation is the only effective treatment for liver failure secondary to primary biliary cirrhosis (II-2).
35. Liver transplantation also may occasionally be indicated in appropriately selected patients for uncontrolled pruritus (III).

Primary Sclerosing Cholangitis

36. Liver transplantation is the only effective treatment for decompensated cirrhosis secondary to primary sclerosing cholangitis (PSC) (II-2).
37. Patients with primary sclerosing cholangitis and cholangiocarcinoma should be excluded from transplantation unless they are enrolled in a clinical trial of experimental therapy (II-3).
38. Because of the high incidence of colon cancer, regularly scheduled colonoscopies should be performed both before and after transplantation in all patients who have inflammatory bowel disease (II-3).

Childhood Cholestatic Diseases

39. Liver transplantation is indicated in appropriately selected children with biliary atresia if portoenterostomy is unsuccessful, or if intractable portal hypertension or liver failure develops despite successful portoenterostomy (III).
40. Liver transplantation should be considered for its ability to significantly prolong survival and improve quality of life by reducing pruritus in syndromic and nonsyndromic forms of intrahepatic cholestasis in children (III).
41. Children with Alagille syndrome should have preoperative assessment for congenital heart disease, which is common in this condition (III).
42. In evaluating patients with cystic fibrosis for liver transplantation, careful assessment of lung disease should be performed (III).

Metabolic Diseases

Alpha-1-Antitrypsin Disease

43. Liver transplantation is the only effective treatment for decompensated cirrhosis secondary to alpha-1-antitrypsin deficiency (II-3).
44. Careful assessment for lung disease should be performed before transplantation in patients with cirrhosis secondary to alpha-1-antitrypsin deficiency, although coexistent disease is uncommon (III).

Wilson Disease

45. Urgent liver transplantation is the only effective option for patients with fulminant hepatic failure resulting from Wilson disease (II-3).
46. Liver transplantation also is indicated for patients with decompensated chronic disease who fail to respond to medical therapy (II-2).
47. Liver transplantation is not recommended as primary treatment for neurological Wilson disease because the liver disease is stabilized by medical therapy in most of these individuals, and outcomes with liver transplantation are not always beneficial (III).

Nonalcoholic Steatohepatitis and Cryptogenic Cirrhosis

48. Liver transplantation should be considered for selected patients with decompensated cirrhosis secondary to nonalcoholic steatohepatitis (NASH). The posttransplantation care of these patients should include metabolic monitoring (III).
49. Liver transplantation should be considered for selected patients with decompensated cryptogenic cirrhosis. These patients should be screened for metabolic dysregulation because of the possibility of underlying nonalcoholic steatohepatitis (III).

Hereditary Hemochromatosis

50. All patients with newly diagnosed cirrhosis should be screened for hemochromatosis using serologic tests, with genetic testing in equivocal cases (III).

51. Survival of transplanted patients with hereditary hemochromatosis is lower than in those transplanted for other causes of liver disease. Due to the increased risk of cardiac complications, a pretransplantation cardiac evaluation is essential (II-3).
52. Efforts should be made to phlebotomize these patients before transplantation (III).

Neonatal Hemochromatosis

53. Liver transplantation is the only effective treatment for infants with severe neonatal hemochromatosis. Urgent evaluation at a transplant center is recommended (II-3).

Tyrosinemia and Glycogen Storage Disease

54. Children with tyrosinemia who develop hepatocellular carcinoma (HCC) and meet the criteria for liver transplantation for HCC should be high-priority candidates (II-3).
55. Children with tyrosinemia and glycogen storage diseases unresponsive to medical management should be considered for transplantation (II-3).
56. Consideration of extrahepatic complications of the underlying disease must be carefully considered in potential transplant candidates (III).

Metabolic Diseases with Severe Extrahepatic Manifestations

Amyloidosis and Hyperxaluria

57. Patients with amyloidosis should be considered for liver transplantation to correct the underlying metabolic defect before end organ damage has occurred (II-3).
58. Liver transplantation, with or without combined kidney transplantation, is curative for hyperoxaluria and should be considered for patients with this disease (II-3).

Urea Cycle and Branched-Chain Amino Acid Disorders

59. Liver transplantation is indicated in children with metabolic diseases that cause progressive extra-hepatic injury resulting in significant morbidity and mortality that are not responsive to disease-specific medications or dietary modification and for which liver transplantation would result in the reversal of the enzyme deficiency and metabolic derangement (II-3).
60. Living related transplantation should be considered only if the enzyme activity of the donor would satisfactorily reverse the deficiency of the recipient (III).
61. The degree of neurological injury before transplantation should be considered when selecting patients for liver transplantation (III).

Hepatic Malignancies

Hepatocellular Carcinoma (HCC)

62. Liver transplantation should be viewed as the treatment of choice for selected patients with HCC who are not candidates for surgical resection and in whom malignancy is confined to the liver (II-2).
63. Optimal results following transplantation are achieved in patients with a single lesion 2 cm or larger and less than 5 cm, or no more than three lesions, the largest of which is less than 3 cm, and no radiographic evidence of extrahepatic disease (II-2).
64. For ideal outcomes, patients who meet these criteria should receive a donor organ within 6 months of listing for transplantation (II-2).

Hepatoblastoma

65. Liver transplantation should be considered for children in whom hepatoblastoma is confined to the liver and is not resectable (II-3).

Fibrolamellar Hepatocellular Carcinoma and Hemangiondothelioma

66. When the tumor is not resectable, liver transplantation should be considered for patients with fibrolamellar HCC, if there is no evidence of extrahepatic disease (III).
67. When the tumor is not resectable, liver transplantation should be considered for patients with epithelioid hemangioendothelioma (III).

Cholangiocarcinoma

68. Transplantation in patients with cholangiocarcinoma should be confined to a few centers with well-designed clinical trials (III).

Fulminant Hepatic Failure

69. Patients with fulminant hepatic failure (FHF) should be referred to a transplant center as quickly as possible for expectant critical care management (III).
70. Patients predicted to have little chance of spontaneous recovery should undergo transplantation as soon as possible (II-3).

Miscellaneous Conditions

Budd-Chiari Syndrome

71. Because there are a variety of effective options available, the selection of patients for liver transplantation for Budd-Chiari syndrome must be individualized, considering alternative therapeutic options (III).

Metastatic Neuroendocrine Tumors

72. Liver transplantation for metastatic neuroendocrine tumors should be confined to highly selected patients who are not candidates for surgical resection in whom symptoms have persisted despite optimal medical therapy (III).

Polycystic Liver Disease

73. Liver transplantation is occasionally indicated for patients with polycystic disease (III).

Retransplantation

74. Liver retransplantation, which is the only means of prolonging life in patients whose initial graft has failed, makes an important contribution to overall survival and should be considered in selected patients with primary graft failure, hepatic artery thrombosis, severe rejection, or recurrent disease (II-3). However, retransplantation is associated with diminished survival and increased costs compared with primary transplantation.
75. Retransplantation should be considered before patients develop severe hepatic and renal failure (II-3).
76. Retransplantation should be used with discretion in the emergency setting and should be avoided in subgroups of patients with little chance of success (III).

Definitions:

Quality of Evidence

Grade I: Randomized controlled trials

Grade II-1: Controlled trials without randomization

Grade II-2: Cohort or case-control analytic studies

Grade II-3: Multiple time series, dramatic uncontrolled experiments

Grade III: Opinions of respected authorities, descriptive epidemiology

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is specifically stated for each recommendation (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Extended survival with excellent quality of life after transplantation in patients with end-stage liver disease
- Liver transplantation has had a profound impact on the care of patients with end-stage liver disease and is the most effective treatment for many patients with acute or chronic liver failure resulting from a variety of causes.

POTENTIAL HARMS

- Rejection, graft failure, and need for retransplantation
- A number of complications can be anticipated after liver transplantation, including perioperative and surgical complications, immunologic and infectious disorders, and a variety of medical complications.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Severe pulmonary hypertension is associated with high perioperative mortality and, if not successfully treated, is a contraindication to liver transplantation.
- Morbid obesity should be considered a contraindication to liver transplantation.
- The most frequently encountered contraindication to transplantation is continued destructive behavior resulting from drug and alcohol addiction.
- The most commonly encountered surgical contraindication to liver transplantation is absence of a viable splanchnic venous inflow system, either from portal vein thrombosis or cavernous transformation of the portal vein in children. Thrombosis of the main portal vein can be successfully bypassed; however, if the entire portal venous system is occluded or atrophied, attempts at transplantation are associated with a high risk of graft loss and perioperative mortality.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Intended for use by physicians, the recommendations in this document suggest preferred approaches to the diagnostic, therapeutic and preventive aspects of care. They are intended to be flexible, in contrast to standards of care, which are inflexible policies to be followed in every case. Specific recommendations are based on relevant published information. Specific recommendations are based on relevant published information. In an attempt to characterize the quality of evidence supporting recommendations, the Practice Guidelines Committee of the American Association for the Study of Liver Diseases (AASLD) requires a category to be assigned and reported with each recommendation (See "Rating Scheme for the Strength of the Evidence" field). These recommendations are fully endorsed by the AASLD.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Murray KF, Carithers RL Jr. AASLD practice guidelines: evaluation of the patient for liver transplantation. Hepatology 2005 Jun;41(6):1407-32. [328 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Jan (revised 2005 Jun)

GUIDELINE DEVELOPER(S)

American Association for the Study of Liver Diseases - Private Nonprofit Research Organization

SOURCE(S) OF FUNDING

American Association for the Study of Liver Diseases

GUIDELINE COMMITTEE

Practice Guidelines Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Potential conflict of interest: Nothing to report

GUIDELINE STATUS

This is the current release of the guideline.

The guideline updates a previous version: Carithers RL Jr. Liver transplantation. American Association for the Study of Liver Diseases. Liver Transpl 2000 Jan;6(1):122-35.

GUIDELINE AVAILABILITY

Electronic copies: Available in portable Document Format (PDF) from the American Association for the Study of Liver Diseases Web site.

Print copies: Available from the American Association for the Study of Liver Diseases, 1729 King Street, Suite 200; Alexandria, VA 22314; Phone: 703-299-9766; Web site: www.aasld.org; e-mail: aasld@aasld.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 9, 2003. The information was verified by the guideline developer on June 12, 2003. This NGC summary was updated by ECRI on July 12, 2005.

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